

-2-

**Amendments to the Claims**

Please cancel Claims 1, 24, 47 and 66. Please amend Claims 2, 25, 48 and 67. The Claim Listing below will replace all prior versions of the claims in the application:

**Claim Listing**

1. Canceled.
2. (Currently amended) A method of substantially preventing modification of a synthetic oligonucleotide or oligonucleotide analog during ~~cleavage~~ removal of at least one  $\beta$ -cyanoethyl protecting group from the oligonucleotide or oligonucleotide analog, comprising the step of contacting a  $\beta$ -cyanoethyl protected oligonucleotide or oligonucleotide analog with an aqueous basic solution ~~comprising at least one substituted or unsubstituted sterically hindered primary aliphatic amine~~ under conditions sufficient to remove at least one  $\beta$ -cyanoethyl protecting group, wherein the aqueous basic solution comprises at least one substituted or unsubstituted sterically hindered primary aliphatic amine.
- 3-5. Canceled.
6. (Original) The method of Claim 2, wherein the  $\beta$ -cyanoethyl protecting groups are removed from a phosphate triester oligonucleotide.
7. (Original) The method of Claim 2, wherein the  $\beta$ -cyanoethyl protecting groups are removed from a phosphorothioate oligonucleotide analog.
8. (Original) The method of Claim 2, wherein the synthetic oligonucleotide or oligonucleotide analog is attached to a solid support by a covalent bond.
9. (Previously presented) The method of Claim 8, wherein the solid support is controlled-

-3-

pore glass, polystyrene or poly(acrylamide).

10. (Previously presented) The method of Claim 8, wherein the oligonucleotide or oligonucleotide analog is cleaved from the solid support.
11. Canceled.
12. (Previously presented) The method of Claim 2, wherein the sterically hindered primary aliphatic amine is *t*-butylamine.
13. (Original) The method of Claim 2, wherein the basic solution comprises an alkali metal hydroxide or an alkaline earth metal hydroxide.
14. (Original) The method of Claim 2, wherein the basic solution is an ammonium hydroxide solution.
15. (Original) The method of Claim 14, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 100°C.
16. (Original) The method of Claim 15, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 35°C.
17. (Original) The method of Claim 16, wherein the temperature of the ammonium hydroxide solution is about 25°C.
18. (Original) The method of Claim 14, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 48 hours.
19. (Original) The method of Claim 18, wherein the synthetic oligonucleotide or

-4-

oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 2 hours.

20. (Previously presented) The method of Claim 2, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 5%.
21. (Previously presented) The method of Claim 20, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 25%.
22. (Previously presented) The method of Claim 21, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 50%.
23. (Original) The method of Claim 22, wherein all the nucleobases are thymine or guanine.
24. Canceled.
25. (Currently amended) A method of substantially preventing modification of a synthetic oligonucleotide or oligonucleotide analog during cleavage removal of at least one  $\beta$ -cyanoethyl protecting group and at least one nucleobase protecting group from the oligonucleotide or oligonucleotide analog, comprising the step of contacting a  $\beta$ -cyanoethyl protected oligonucleotide or oligonucleotide analog with an aqueous basic solution comprising at least one substituted or unsubstituted sterically hindered primary aliphatic amine under conditions sufficient to remove at least one  $\beta$ -cyanoethyl protecting group and at least one nucleobase protecting group, wherein the aqueous basic solution comprises at least one substituted or unsubstituted sterically hindered primary aliphatic amine.

-5-

26-28. Canceled.

29. (Previously presented) The method of Claim 25, wherein the  $\beta$ -cyanoethyl protecting groups and the nucleobase protecting groups are removed from a phosphate diester oligonucleotide.
30. (Previously presented) The method of Claim 25, wherein the  $\beta$ -cyanoethyl protecting groups and the nucleobase protecting groups are removed from a phosphorothioate oligonucleotide analog.
31. (Original) The method of Claim 25, wherein the synthetic oligonucleotide or oligonucleotide analog is attached to a solid support by a covalent bond.
32. (Original) The method of Claim 31, wherein the solid support is controlled-pore glass, polystyrene or poly(acrylamide).
33. (Previously presented) The method of Claim 31, wherein the oligonucleotide or oligonucleotide analog is cleaved from the solid support.
34. Canceled.
35. (Previously presented) The method of Claims 25, wherein the sterically hindered primary aliphatic amine is *t*-butylamine.
36. (Original) The method of Claim 25, wherein the basic solution comprises an alkali metal hydroxide or an alkaline earth metal hydroxide.
37. (Original) The method of Claim 25, wherein the basic solution is an ammonium hydroxide solution.

-6-

38. (Original) The method of Claim 37, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 100°C.
39. (Original) The method of Claim 38, wherein the temperature of the ammonium hydroxide solution is about 45°C to about 65°C.
40. (Original) The method of Claim 39, wherein the temperature of the ammonium hydroxide solution is about 55°C.
41. (Original) The method of Claim 37, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 48 hours.
42. (Original) The method of Claim 41, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 6 hours to about 16 hours.
43. (Previously presented) The method of Claim 25, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 5%.
44. (Previously presented) The method of Claim 43, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 25%.
45. (Previously presented) The method of Claim 44, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 50%.
46. (Original) The method of Claim 45, wherein all the nucleobases are thymine or guanine

-7-

47. Canceled.

48. (Currently amended) A method of substantially preventing modification of a synthetic oligonucleotide or oligonucleotide analog during ~~cleavage removal~~ of at least one  $\beta$ -cyanoethyl protecting group and at least one nucleobase protecting group from the oligonucleotide or an oligonucleotide analog, comprising the step of contacting a  $\beta$ -cyanoethyl protected oligonucleotide or oligonucleotide analog with an ammonium hydroxide solution, wherein the solution contains containing *t*-butylamine, and wherein the contact is under conditions sufficient to remove at least one nucleobase protecting group and at least one  $\beta$ -cyanoethyl protecting group.

49-51. Canceled.

52. (Original) The method of Claim 48, wherein a the  $\beta$ -cyanoethyl protecting groups and the nucleobase protecting groups are removed from a phosphate triester oligonucleotide.

53. (Original) The method of Claim 48, wherein a the  $\beta$ -cyanoethyl protecting groups and the nucleobase protecting groups are removed from a phosphorothioate oligonucleotide analog.

54. (Original) The method of Claim 48, wherein the synthetic oligonucleotide or oligonucleotide analog is attached to a solid support by a covalent bond.

55. (Original) The method of Claim 54, wherein the solid support is controlled-pore glass, polystyrene or poly(acrylamide).

56. (Previously presented) The method of Claim 54, wherein the oligonucleotide or oligonucleotide analog is cleaved from the solid support.

-8-

57. (Original) The method of Claim 48, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 100°C.
58. (Original) The method of Claim 57, wherein the temperature of the ammonium hydroxide solution is about 45°C to about 65°C.
59. (Original) The method of Claim 58, wherein the temperature of the ammonium hydroxide solution is about 55°C.
60. (Original) The method of Claim 48, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 48 hours.
61. (Original) The method of Claim 60, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 6 hours to about 16 hours.
62. (Previously presented) The method of Claim 48, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 5%.
63. (Previously presented) The method of Claim 62, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 25%.
64. (Previously presented) The method of Claim 63, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 50%.
65. (Original) The method of Claim 64, wherein all the nucleobases are thymine or guanine.

-9-

66. Canceled.

67. (Currently amended) A method of producing an oligonucleotide or oligonucleotide analog, wherein modification of the oligonucleotide or oligonucleotide analog during cleavage removal of at least one  $\beta$ -cyanoethyl protecting group is substantially prevented, comprising the steps of:

- a) synthesizing an oligonucleotide or oligonucleotide analog having at least one  $\beta$ -cyanoethyl protecting group; and
- b) contacting the  $\beta$ -cyanoethyl protected oligonucleotide or oligonucleotide analog with an aqueous basic solution, wherein the solution comprises comprising at least one substituted or unsubstituted sterically hindered primary aliphatic amine, and wherein the contact is under conditions sufficient to remove at least one  $\beta$ -cyanoethyl protecting group, whereby the  $\beta$ -cyanoethyl protecting group is removed without substantially modifying the oligonucleotide or oligonucleotide analog.

68-70. Canceled.

71. (Original) The method of Claim 67, wherein the synthetic oligonucleotide or oligonucleotide analog is synthesized using phosphoramidite chemistry.

72. (Previously presented) The method of Claim 71, wherein at least one nucleobase protecting group is cleaved when the synthetic oligonucleotide or oligonucleotide analog is contacted with the aqueous basic solution.

73. (Original) The method of Claim 67, wherein the oligonucleotide produced is a phosphate diester oligonucleotide.

74. (Original) The method of Claim 67, wherein a the oligonucleotide analog produced is a



-10-

phosphorothioate oligonucleotide analog.

75. (Original) The method of Claim 67, wherein the synthetic oligonucleotide or oligonucleotide analog is attached to a solid support by a covalent bond.
76. (Original) The method of Claim 75, wherein the solid support is controlled-pore glass, polystyrene or poly(acrylamide).
77. (Previously presented) The method of Claim 75, wherein the oligonucleotide or oligonucleotide analog is cleaved from the solid support.
78. Canceled.
79. (Currently amended) The method of Claim 67, wherein the sterically hindered primary aliphatic amine is *t*-butylamine.
80. (Original) The method of Claim 67, wherein the basic solution comprises an alkali metal hydroxide or an alkaline earth metal hydroxide.
81. (Original) The method of Claim 67, wherein the basic solution is an ammonium hydroxide solution.
82. (Original) The method of Claim 81, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 100°C.
83. (Original) The method of Claim 82, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 35°C.
84. (Original) The method of Claim 83, wherein the temperature of the ammonium hydroxide solution is about 25°C.

-11-

85. (Original) The method of Claim 81, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 48 hours.
86. (Previously presented) The method of Claim 85, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 2 hours.
87. (Original) The method of Claim 72, wherein the basic solution is an ammonium hydroxide solution.
88. (Original) The method of Claim 87, wherein the temperature of the ammonium hydroxide solution is about 20°C to about 100°C.
89. (Original) The method of Claim 88, wherein the temperature of the ammonium hydroxide solution is about 45°C to about 65°C.
90. (Original) The method of Claim 89, wherein the temperature of the ammonium hydroxide solution is about 55°C.
91. (Original) The method of Claim 87, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 0.5 hours to about 48 hours.
92. (Original) The method of Claim 91, wherein the synthetic oligonucleotide or oligonucleotide analog is contacted with the ammonium hydroxide solution for about 6 hours to about 16 hours.
93. (Previously presented) The method of Claim 72, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide

-12-

analog is at least about 5%.

94. (Previously presented) The method of Claim 93, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 25%.
- 95 (Previously presented) The method of Claim 94, wherein the combined percentage of nucleobases which are thymine and guanine in the oligonucleotide or oligonucleotide analog is at least about 50%.
96. (Original) The method of Claim 95, wherein all the nucleobases are thymine or guanine.
97. (Previously presented) A method of preparing an oligonucleotide or oligonucleotide analog comprising removing at least one  $\beta$ -cyanoethyl group from a  $\beta$ -cyanoethyl protected oligonucleotide or oligonucleotide analog using the method of any one preceding claim.